L Number	Hits	Search Text	DB	Time stamp
1	3191	514/54	USPAT; US-PGPUB; EPO; DERWENT	2003/07/24 08:07
2	766	514/54 and dextran	USPAT; US-PGPUB; EPO; DERWENT	2003/07/24 08:07
3	0	(514/54 and dextran) and methylcarboxyl$	USPAT; US-PGPUB; EPO; DERWENT	2003/07/24 08:08
4	0	(514/54 and dextran) and methylcarboxylate	USPAT; US-PGPUB; EPO; DERWENT	2003/07/24 08:08
5	766	(514/54 and dextran) andcarboxymethyl	USPAT; US-PGPUB; EPO; DERWENT	2003/07/24 08:08
6	207	(514/54 and dextran) and carboxymethyl	USPAT; US-PGPUB; EPO; DERWENT	2003/07/24 08:09
7	0	((514/54 and dextran) and carboxymethyl) and carboxymethylbenzylamide	USPAT; US-PGPUB; EPO; DERWENT	2003/07/24 08:09
8	0	((514/54 and dextran) and carboxymethyl) and methylcarboxybenzylamide	USPAT; US-PGPUB; EPO; DERWENT	2003/07/24 08:09
9	156	((514/54 and dextran) and carboxymethyl) and (sulfate or sulphate)	USPAT; US-PGPUB; EPO; DERWENT	2003/07/24 08:11
10	148	(((514/54 and dextran) and carboxymethyl) and (sulfate or sulphate)) and composition	USPAT; US-PGPUB; EPO; DERWENT	2003/07/24 08:11
11	64	((((514/54 and dextran) and carboxymethyl) and (sulfate or sulphate)) and composition) and excipient	USPAT; US-PGPUB; EPO; DERWENT	2003/07/24 08:14
12	472	514/59	USPAT; US-PGPUB; EPO; DERWENT	2003/07/24 08:14
13	324	514/59 and dextran	USPAT; US-PGPUB; EPO; DERWENT	2003/07/24 08:15
14	1	(514/59 and dextran) and methylcarboxylate	USPAT; US-PGPUB; EPO; DERWENT	2003/07/24 08:16
15	324	(514/59 and dextran) andcarboxymethylbenzylamide	USPAT; US-PGPUB; EPO; DERWENT	2003/07/24 08:16
16	2	(514/59 and dextran) and carboxymethylbenzylamide	USPAT; US-PGPUB; EPO; DERWENT	2003/07/24 08:18
17	2	((514/59 and dextran) and carboxymethylbenzylamide) and (sulfate or sulphate)	USPAT; US-PGPUB; EPO; DERWENT	2003/07/24 08:22

18	210	536/51	USPAT; US-PGPUB; EPO; DERWENT	2003/07/24 08:22
19	138	536/51 and dextran	USPAT; US-PGPUB; EPO; DERWENT	2003/07/24 08:23
20	0	(536/51 and dextran) and methylcarboxylate	USPAT; US-PGPUB; EPO; DERWENT	2003/07/24 08:23
22	0	((536/51 and dextran) and (sulfate or sulphate)) and carboxymethylbenzylamide	USPAT; US-PGPUB; EPO; DERWENT	2003/07/24 08:24
21	72	(536/51 and dextran) and (sulfate or sulphate)	USPAT; US-PGPUB; EPO; DERWENT	2003/07/24 08:24

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 NEWS 20  May 19   RAPRA enhanced with new search field, simultaneous left and
                   right truncation
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=> s dextran
L1 108349 DEXTRAN

=> s l1 and (derivat? or functional)
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=> s l1 and (derivat? or functional?)
18 FILES SEARCHED...
L2 45437 L1 AND (DERIVAT? OR FUNCTIONAL?)

=> s l2 and (methylcarboxyl or carboxymethyl?)
L3 13447 L2 AND (METHYLCARBOXYL OR CARBOXYMETHYL?)

=> s l3 and carboxymethylbenzylamide
L4 17 L3 AND CARBOXYMETHYLBENZYLAMIDE

=> s l4 and (sulfat? or sulphat?)
L5 8 L4 AND (SULFAT? OR SULPHAT?)

=> dis l5 1-8 bib abs

L5 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1997:108422 CAPLUS
DN 126:220468
TI Mechanism of thrombin inhibition by heparin cofactor II in the presence of dermatan **sulfates**, native or oversulfated, and a heparin-like **dextran derivative**
AU Maaroufi, Raoui M.; Jozefowicz, Marcel; Tapon-Bretaudiere, Tapon; Jozefonvicz, Jacqueline; Fischer, Anne-Marie
CS Lab. Hematolgie, CHU Necker-Enfants Malades, Paris, 75743, Fr.
SO Biomaterials (1997), 18(4), 359-366
CODEN: BIMADU; ISSN: 0142-9612
PB Elsevier
DT Journal
LA English
AB The kinetics of thrombin inhibition by heparin cofactor II (HC II) in the presence of dermatan **sulfatees**, native (DS), or oversulfated (DSS 1 and DSS 2) and a biospecific **dextran deriv.** substituted with **carboxymethyl**, **carboxymethyl** -benzylamide and **carboxymethyl** benzylamide-sulfonate **functional** groups (CMDBS), has been studied as a function of the **sulfated** polysaccharide concn. The initial HC II and thrombin concns. were set at equimolar levels. Anal. of the exptl. data obtained for DS, DSS1 and DSS2 was performed using a previously described model which allows computation of the dissocn. const. (KPS,HC) of the

polysaccharide-HC II complex and the rate const. of thrombin inhibition by the polysaccharide-HC II complex (k). A KPS,HC of 9.6.times.10-7M and a k of 4.5.times.109M-1 were found for DS, whereas KPS,HC 2.1.times.10-6M, k 1.1.times.1010M-1min-1 and KPS,HC 4.3.times.10-7M, k 1.4.times.1010M-1min-1 were found for DSS1 and DSS2, resp. Knowing that DSS1 has a sulfur content per disaccharide of 7.8%, compared with 11.5% for DDS2, these results indicate that the polysaccharide affinity for HC II is increased only in the case of DSS 2, whereas the oversulfation increases the reactivities towards thrombin of both complexes DSS1-HC II and DSS2-HC II. A better conformation of these complexes may favor a faster interaction with the protease. Unlike heparin, DS at concns. higher than 10-5M does not modify the reaction rate of thrombin inhibition, a fact which can be explained by the absence of complex formation between DS and thrombin. The exptl. data obtained for CMDBS fit a kinetic model in which the biospecific **dextran deriv**. rapidly forms a complex with thrombin which is more reactive towards HC II than the free protease. The reaction rate remained unchanged for CMDBS concns. equal to or higher than 10-5M, whereas CMDBS was found to interfere strongly with the fibrinogen-thrombin interaction. These data suggests that CMDBS has a strong affinity for the protease and no affinity for HC II. The computed dissocn. const. of the CMDBS-thrombin complex (KPS,E) WAS 2.4.times.10-7M and the rate const. of the reaction of this complex with HC II(k) was 1.7.times.109M-1min-1. These findings indicate that CMDBS exerts its catalytic effect through a unique mechanism of action and may constitute a new class of anticoagulant drugs.

L5 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1996:155196 CAPLUS
DN 124:220975
TI FGF protection and inhibition of human neutrophil elastase by **carboxymethyl** benzylamide sulfonate **dextran derivatives**
AU Meddahi, Anne; Lemdjabar, Hassan; Caruelle, Jean-Pierre; Barritault, Denis; Hornebeck, William
CS Lab. Recherche Croissance Regeneration Tissulaires, Univ. Paris XII-Val de Marne, Creteil, F94010, Fr.
SO International Journal of Biological Macromolecules (1996), 18(1,2), 141-5
CODEN: IJBMDR; ISSN: 0141-8130
PB Elsevier
DT Journal
LA English
AB Several **derivatized dextrans** (DxD) contg. defined percentage of **carboxymethyl**, **carboxymethyl** benzylamide and **carboxymethyl** benzylamide sulfonate groups have been shown to stimulate tissue repair in various in vivo models including skin, bone, muscle and cornea. These selected DxD were also shown to mimic heparin or heparan **sulfate** by their ability to interact with, stabilize and protect the heparin-binding growth factor of the fibroblast growth factor family against trypsin digestion. The wound healing action of these DxD was explained by postulating that the endogenously released heparin-binding growth factors could be protected within the wound. To further understand the action of these DxD on tissue repair, the authors have studied their effect on the human neutrophil elastase (HNE) activity, one of the proteases involved in wound repair. These DxD inhibited HNE in an hyperbolic non-competitive manner. Extent of HNE inhibition by DxD increased with their mol. wt. and benzylamide sulfonate substitution levels. One DxD, RGT11, was the best inhibitor (Ki 40 pM) and efficiently inhibited FGF-2 proteolysis by HNE, restoring its growth-promoting activity towards human skin fibroblasts. The data contribute to a better understanding of the wound-healing property and anti-inflammatory activity of these polymers.

L5 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1996:59901 CAPLUS

DN 124:164792
TI Heparan-like molecules induce the repair of skull defects
AU Blanquaert, F.; Saffar, J. L.; Colombier, M. L.; Carpentier, G.; Barritault, D.; Caruelle, J. P.
CS CNRS, Univ. Paris XII, Creteil, 94010, Fr.
SO Bone (New York) (1995), 17(6), 499-506
CODEN: BONEDL; ISSN: 8756-3282
PB Elsevier
DT Journal
LA English
AB Heparin-binding growth factors (HBGFs) are known to stimulate bone repair when applied to bone lesions. Nevertheless, successful treatments are obtained with high protein doses since HBGFs are rapidly degraded in situ by multiple proteolytic activities assocd. with the inflammatory period of tissue healing. Like heparin or heparan **sulfates**, heparan-like mols., named **carboxymethyl**-benzylamide-sulfonated **dextrans** (CMDBS), are known to potentiate fibroblast growth factor activities by stabilizing them against pH, thermal or proteolytic denaturations, and by enhancing their binding with cell surface receptors. We have postulated that CMDBS stimulate in vivo bone healing by interacting with endogenous HBGFs, spontaneously released in the wounded site. The effect of CMDBS on bone repair was studied in a skull defect model in rats by computer-assisted radiomorphometry and histomorphometry. Single application of CMDBS in a collagen vehicle to skull defects induced a dose-dependent increase in bone defect closure and new bone formation after 35 days. Complete bony bridging occurred in defects treated with 3 .mu.g CMDBS, whereas bone formation was not obsd. in vehicle-treated defects which contained only dense fibrous connective tissue between the defect margins. These results indicate that heparan-like mols., such as CMDBS, are able to induce bone regeneration of skull defects. This action is possibly mediated by potentiation of endogenous growth factor activities and/or by neutralization of proteolytic activities.

L5 ANSWER 4 OF 8 IFIPAT COPYRIGHT 2003 IFI on STN
AN 10239575 IFIPAT;IFIUDB;IFICDB
TI PHARMACEUTICAL COMPOSITIONS WITH WOUND HEALING OR ANTI-COMPLEMENTARY ACTIVITY COMPRISING A **DEXTRAN DERIVATIVE**
INF Correia; Jose, Saint Amand les Eaux, FR
Dahricorreia; Latifa, Saint Amand les Eaux, FR
Huynh; Remi, Saint Amand les Eaux, FR
Jozefonvicz; Jacqueline, Lamorlaye, FR
Jozefowicz; Marcel, Lamorlaye, FR
IN Correia Jose (FR); Dahricorreia Latifa (FR); Huynh Remi (FR); Jozefonvicz Jacqueline (FR); Jozefowicz Marcel (FR)
PAF Unassigned
PA Unassigned Or Assigned To Individual (68000)
AG Welsh & Katz, Ltd. Thomas W. Tolpin, 22nd Floor, 120 South Riverside Plaza, Chicago IL, 60606, US
PI US 2002183282 A1 20021205
AI US 2001-20044 20011213
PRAI FR 1999-7636 19990616
WO 2000-FR1658 20000615
FI US 2002183282 20021205
DT Utility; Patent Application - First Publication
FS CHEMICAL
APPLICATION
CLMN 21
GI 3 Figure(s).
FIG. 1 diagrammatically illustrates the structure of a **dextran** which is substituted by the different chemical groups which are attached to the glucoside units; the position of the substituent on the different carbons of the glucoside-based units is shown in position 2, by way of example;
FIG. 2 illustrates the anticomplementary activity of a **dextran**

derivative of general formula DMCaBbSuc; in this figure, the CH50 (%), which is measured as indicated in example 5, is depicted in terms of the time (hours);

FIG. 3 shows the healing, after 3 and 7 days (D3 and D7), of dorsal skin incisions which were performed on rats, the wounds being treated either with a physiological solution (photographs in column 1) or with a solution of a **dextran derivative** of general formula DMCaBbSuc (photographs in column 2).

AB The invention concerns pharmaceutical compositions with wound healing or anti-complementary activity, and their uses, said compositions comprising. (1) at least a **dextran derivative** of general formula DMCaBbSuc, a, b, and c respectively representing the degrees of substitution in the groups MC, B and Su, wherein a greater-double-equals 0.6, b=0 or greaterdouble-equals 0.1, and c=0 or ranges widely between 0.1 and 0.5 for a wound healing composition, and a greater-double-equals 0. 3, b greater-double-equals 0.1 and c=0 or ranges widely between 0.1 and 0.4 for a composition with anti-complementary activity; (2) and at least a pharmaceutically acceptable carrier, said **dextran derivative** being present in a single unit dose or at a concentration adapted to the desired wound healing or anticomplementary activity.

CLMN 21 3 Figure(s).

FIG. 1 diagrammatically illustrates the structure of a **dextran** which is substituted by the different chemical groups which are attached to the glucoside units; the position of the substituent on the different carbons of the glucoside-based units is shown in position 2, by way of example;

FIG. 2 illustrates the anticomplementary activity of a **dextran derivative** of general formula DMCaBbSuc; in this figure, the CH50 (%), which is measured as indicated in example 5, is depicted in terms of the time (hours);

FIG. 3 shows the healing, after 3 and 7 days (D3 and D7), of dorsal skin incisions which were performed on rats, the wounds being treated either with a physiological solution (photographs in column 1) or with a solution of a **dextran derivative** of general formula DMCaBbSuc (photographs in column 2).

L5 ANSWER 5 OF 8 IFIPAT COPYRIGHT 2003 IFI on STN
AN 10225413 IFIPAT;IFIUDB;IFICDB
TI BIOLOGICALLY ACTIVE MATERIAL BASED ON AN INSOLUBILISED **DEXTRAN DERIVATIVE** AND A GROWTH FACTOR
INF Blanchat; Cinderella, Margency, FR
Chaubet; Frederic, Eaubonne, FR
Correia; Jose, Saint Amand Les Eaux, FR
Jozefonvicz; Jacqueline, Lamorlaye, FR
Jozefowicz; Marcel, Lamorlaye, FR
Logeart-Avramoglou; Delphine, Groslay, FR
Meunier; Alain, Saint-Mande, FR
Petite; Herve, Paris, FR
Sedel; Laurent, Jouy en Josas, FR
IN Blanchat Cinderella (FR); Chaubet Frederic (FR); Correia Jose (FR); Jozefonvicz Jacqueline (FR); Jozefowicz Marcel (FR); Logeart-Avramoglou Delphine (FR); Meunier Alain (FR); Petite Herve (FR); Sedel Laurent (FR)
PAF Unassigned
PA Unassigned Or Assigned To Individual (68000)
AG Welsh & Katz, Ltd. Thomas W. Tolpin, 22nd Floor, 120 South Riverside Plaza, Chicago IL, 60606, US
PI US 2002169120 A1 20021114
AI US 2001-16706 20011211
PRAI FR 1999-7401 19990611
WO 2000-FR1603 20000609
FI US 2002169120 20021114
DT Utility; Patent Application - First Publication
FS CHEMICAL

APPLICATION
CLMN 23
GI 7 Figure(s).
FIG. 1 schematically illustrates the structure of a **dextran derivative** of general formula DMCaBbSUcSd;
FIG. 2a represents the results of electrophoreses on 0.8% agarose gel of various polymers and of the growth factor TGFbeta 1;
FIG. 2b represents the results of electrophoreses on 0.8% agarose gel of various polymers and of BMP extracted from a bovine bone tissue;
FIGS. 3a and 3b represent the quantity (in pg, cumulative values) of TGF-beta 1 released by the gels T500 (native **dextran**) and FC27 (substituted **dextran derivative**) as a function of time (in hours), without renewal of the medium (FIG. 3a) and with renewal of the medium (FIG. 3b), respectively, according to the protocol described in example 5;
FIG. 4a represents a radiograph of bone neoformation induced in rats by extracted bovine BMP, according to the protocol described in example 9;
FIG. 4b represents a view under an optical microscope of a bone nodule formed at an intramuscular site in a rat, according to the protocol described in example 9;
FIG. 4c represents a view under an optical microscope of an implant based on coral and extracted bovine BMP at an intramuscular site, in a rat, according to the protocol described in example 9.
AB The invention concerns a biologically active material essentially comprising at least an insolubilised **dextran derivative** of general formula DMCaBbSUcSd and at least a growth factor having an activity on osteoarticular, dental and/or maxillofacial tissues, and the method for preparing same. The invention also concerns the uses of said biomaterial for preparing a repair or filing material, such as an implant, for osteoarticular, dental or maxillofacial applications and for preparing an orthopaedic, dental or maxillofacial prosthesis, and the prosthesis coated with said biologically active material.
CLMN 23 7 Figure(s).
FIG. 1 schematically illustrates the structure of a **dextran derivative** of general formula DMCaBbSUcSd;
FIG. 2a represents the results of electrophoreses on 0.8% agarose gel of various polymers and of the growth factor TGFbeta 1;
FIG. 2b represents the results of electrophoreses on 0.8% agarose gel of various polymers and of BMP extracted from a bovine bone tissue;
FIGS. 3a and 3b represent the quantity (in pg, cumulative values) of TGF-beta 1 released by the gels T500 (native **dextran**) and FC27 (substituted **dextran derivative**) as a function of time (in hours), without renewal of the medium (FIG. 3a) and with renewal of the medium (FIG. 3b), respectively, according to the protocol described in example 5;
FIG. 4a represents a radiograph of bone neoformation induced in rats by extracted bovine BMP, according to the protocol described in example 9;
FIG. 4b represents a view under an optical microscope of a bone nodule formed at an intramuscular site in a rat, according to the protocol described in example 9;
FIG. 4c represents a view under an optical microscope of an implant based on coral and extracted bovine BMP at an intramuscular site, in a rat, according to the protocol described in example 9.

L5 ANSWER 6 OF 8 USPATFULL on STN
AN 2002:323116 USPATFULL
TI Pharmaceutical compositions with wound healing or anti-complementary activity comprising a **dextran derivative**
IN Dahricorreia, Latifa, Saint Amand les Eaux, FRANCE
Jozefonvicz, Jacqueline, Lamorlaye, FRANCE
Jozefowicz, Marcel, Lamorlaye, FRANCE
Correia, Jose, Saint Amand les Eaux, FRANCE
Huynh, Remi, Saint Amand les Eaux, FRANCE
PI US 2002183282 A1 20021205

AI US 2001-20044 A1 20011213 (10)
PRAI FR 1999-7636 19990616
WO 2000-FR1658 20000615
DT Utility
FS APPLICATION
LREP Welsh & Katz, Ltd., Thomas W. Tolpin, 22nd Floor, 120 South Riverside Plaza, Chicago, IL, 60606
CLMN Number of Claims: 21
ECL Exemplary Claim: 1
DRWN 3 Drawing Page(s)
LN.CNT 929
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention concerns pharmaceutical compositions with wound healing or anti-complementary activity, and their uses, said compositions comprising. (1) at least a **dextran derivative** of general formula DMC.sub.aB.sub.bSu.sub.c, a, b, and c respectively representing the degrees of substitution in the groups MC, B and Su, wherein a .gtoreq.0.6, b=0 or .gtoreq.0.1, and c=0 or ranges widely between 0.1 and 0.5 for a wound healing composition, and a.gtoreq.0.3, b .gtoreq.0.1 and c=0 or ranges widely between 0.1 and 0.4 for a composition with anti-complementary activity; (2) and at least a pharmaceutically acceptable carrier, said **dextran derivative** being present in a single unit dose or at a concentration adapted to the desired wound healing or anti-complementary activity.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 7 OF 8 USPATFULL on STN
AN 2002:301575 USPATFULL
TI Biologically active material based on an insolubilised **dextran derivative** and a growth factor
IN Blanchat, Cinderella, Margency, FRANCE
Logeart-Avramoglou, Delphine, Groslay, FRANCE
Petite, Herve, Paris, FRANCE
Meunier, Alain, Saint-Mande, FRANCE
Chaubet, Frederic, Eaubonne, FRANCE
Jozefonvicz, Jacqueline, Lamorlaye, FRANCE
Jozefowicz, Marcel, Lamorlaye, FRANCE
Sedel, Laurent, Jouy en Josas, FRANCE
Correia, Jose, Saint Amand Les Eaux, FRANCE
PI US 2002169120 A1 20021114
AI US 2001-16706 A1 20011211 (10)
PRAI FR 1999-7401 19990611
WO 2000-FR1603 20000609
DT Utility
FS APPLICATION
LREP Welsh & Katz, Ltd., Thomas W. Tolpin, 22nd Floor, 120 South Riverside Plaza, Chicago, IL, 60606
CLMN Number of Claims: 23
ECL Exemplary Claim: 1
DRWN 4 Drawing Page(s)
LN.CNT 983
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention concerns a biologically active material essentially comprising at least an insolubilised **dextran derivative** of general formula DMC.sub.aB.sub.bSU.sub.cS.sub.d and at least a growth factor having an activity on osteoarticular, dental and/or maxillofacial tissues, and the method for preparing same. The invention also concerns the uses of said biomaterial for preparing a repair or filing material, such as an implant, for osteoarticular, dental or maxillofacial applications and for preparing an orthopaedic, dental or maxillofacial prosthesis, and the prosthesis coated with said biologically active material.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 8 OF 8 WPINDEX COPYRIGHT 2003 THOMSON DERWENT on STN
AN 1999-385580 [32] WPINDEX
DNC C1999-113486
TI New **dextran derivatives** with anticoagulant and antithrombotic activity.
DC B04
IN CHAUBET, F; CORREIA, J; DAHRI, L; HUYNH, R; JOZEFOWICZ, J; JOZEFOWICZ, M; JOZEFONVICZ, J
PA (SOLU-N) SOLUTIONS SA; (SOLU-N) SOLUTIONS
CYC 77
PI WO 9929734 A1 19990617 (199932)* FR 46p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AU BA BB BG BR CA CN CU CZ EE GD GE HR HU ID IL IN IS JP KG KP KR LC LK LR LT LV MG MK MN MX NO NZ PL RO SG SI SK SL TR TT UA US UZ VN YU ZW
FR 2772382 A1 19990618 (199932)
AU 9915677 A 19990628 (199946)
EP 990002 A1 20000405 (200021) FR
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
JP 2001523300 W 20011120 (200204) 49p
ADT WO 9929734 A1 WO 1998-FR2699 19981211; FR 2772382 A1 FR 1997-15702 19971211; AU 9915677 A AU 1999-15677 19981211; EP 990002 A1 EP 1998-959962 19981211, WO 1998-FR2699 19981211; JP 2001523300 W WO 1998-FR2699 19981211, JP 1999-530262 19981211
FDT AU 9915677 A Based on WO 9929734; EP 990002 A1 Based on WO 9929734; JP 2001523300 W Based on WO 9929734
PRAI FR 1997-15702 19971211
AN 1999-385580 [32] WPINDEX
AB WO 9929734 A UPAB: 19990813
NOVELTY - New **derivatives** of **dextran** (I) which have medical use with specific biological action.
DETAILED DESCRIPTION - **Dextran derivatives** of formula DMCaBbSucSd (I) are new.
D = polysaccharide chain, preferably formed by chains of glucoside units;
MC = methylcarboxylate groups;
B = **carboxymethylbenzylamide** groups;
Su = **sulphate** groups;
S = sulphonate groups;
a-d = degree of substitution (ds), in groups MC, B, Su and S respectively, expressed as the ratio to the number of free hydroxyl groups in the glucoside unit of the **dextran**;
a = 0 or is greater than or equal to 0.3;
b = 0 or is greater than or equal to 0.1;
c = 0 or greater than or equal to 0.1;
d = 0 or less than or equal to 0.15;
provided that when d = 0, then a and/or b are not zero.
(I) have homogeneity in:
(a) the distribution of chain size illustrated by a gaussian elution profile symmetrical in high performance steric exclusion chromatography;
(b) the distribution of charged chemical groups illustrated by an elution profile with a single symmetrical peak in low pressure ion-exchange chromatography.
INDEPENDENT CLAIMS are also included for:
(1) medicaments comprising (I) as active agent, optionally with another active agent and/or at least one active agent vehicle and/or a support, preferably a liposome;
(2) the preparation of (I);
(3) **dextran carboxymethyl** benzylamide of formula DMCaBb (II) where a and b are both other than 0, as intermediate for (I);

and

(4) **dextran** benzylamide as intermediate for (I).

ACTIVITY - Cicatrizant; anticoagulant; anti-complementary agent.

Anticoagulant activity was measured using the time of activity of cephalin. DMCBSu1 had anticoagulant activity of 0.02 IU/mg compared to 4.0 IU/mg for DMCBSu3 and 173 IU/mg for heparin.

MECHANISM OF ACTION - None given.

USE - (II) is useful as an agent with anti-complementary activity (claimed). (I) are useful as plasma substitutes and for modulating cellular proliferation.

The following uses are claimed:

(1) (I) in which a is greater than or equal to 0.6, b is not zero, c is 0 or less than or equal to 0.5, and d is less than or equal to 0.15 or 0 and the molar mass is 3000 -500 000 g/mole, are useful as cicatrizants;

(2) (I) in which a is greater than or equal to 0.3, b is not 0, c is 0 or less than or equal to 0.4, and d is less than or equal to 0.15 or 0, with a molar mass of 10000-60000 g/mole have anti-complementary activity and are plasma substitutes;

(3) (I) in which a is greater than or equal to 0.5, b is not 0, c is 0 or less than or equal to 0.4, d is less than or equal to 0.15 or 0 and the molar mass is 3000-100000 g/mole, are for modulating cellular proliferation;

(4) (I) in which a is greater than or equal to 0.4, b is not 0, c is greater than or equal to 0.3 and d is less than or equal to 0.15 or 0, with a molar mass of 3000-20000 g/mole, are useful as anticoagulants.

ADVANTAGE - The process enables the degree of substitution of the dextran, the homogeneity of the distribution of chemical groups and the homogeneity of the size of the polysaccharide chains of the product to be controlled, giving improved reproducibility. The process uses less steps than in the prior art and gives improved yields, e.g. 80% for stages (a) and (b) and 60% for stage (c).

Dwg.1/3

=> dis l4 1-17 bib abs

L4 ANSWER 1 OF 17 CAPLUS COPYRIGHT 2003 ACS on STN

AN 1997:108422 CAPLUS

DN 126:220468

TI Mechanism of thrombin inhibition by heparin cofactor II in the presence of dermatan sulfates, native or oversulfated, and a heparin-like **dextran derivative**

AU Maaroufi, Raoui M.; Jozefowicz, Marcel; Tapon-Bretaudiere, Tapon; Jozefonvicz, Jacqueline; Fischer, Anne-Marie

CS Lab. Hematolgie, CHU Necker-Enfants Malades, Paris, 75743, Fr.

SO Biomaterials (1997), 18(4), 359-366
CODEN: BIMADU; ISSN: 0142-9612

PB Elsevier

DT Journal

LA English

AB The kinetics of thrombin inhibition by heparin cofactor II (HC II) in the presence of dermatan sulfatees, native (DS), or oversulfated (DSS 1 and DSS 2) and a biospecific **dextran deriv.** substituted with **carboxymethyl**, **carboxymethyl**-benzylamide and **carboxymethyl** benzylamide-sulfonate **functional** groups (CMDBS), has been studied as a function of the sulfated polysaccharide concn. The initial HC II and thrombin concns. were set at equimolar levels. Anal. of the exptl. data obtained for DS, DSS1 and DSS2 was performed using a previously described model which allows computation of the dissocn. const. (KPS,HC) of the polysaccharide-HC II complex and the rate const. of thrombin inhibition by the polysaccharide-HC II complex (k). A KPS,HC of 9.6.times.10-7M and a k of 4.5.times.109M-1 were found for DS, whereas KPS,HC 2.1.times.10-6M, k 1.1.times.1010M-1min-1 and KPS,HC 4.3.times.10-7M, k 1.4.times.1010M-1min-1 were found for DSS1 and

DSS2, resp. Knowing that DSS1 has a sulfur content per disaccharide of 7.8%, compared with 11.5% for DDS2, these results indicate that the polysaccharide affinity for HC II is increased only in the case of DSS 2, whereas the oversulfation increases the reactivities towards thrombin of both complexes DSS1-HC II and DSS2-HC II. A better conformation of these complexes may favor a faster interaction with the protease. Unlike heparin, DS at concns. higher than 10-5M does not modify the reaction rate of thrombin inhibition, a fact which can be explained by the absence of complex formation between DS and thrombin. The exptl. data obtained for CMDBS fit a kinetic model in which the biospecific **dextran deriv**. rapidly forms a complex with thrombin which is more reactive towards HC II than the free protease. The reaction rate remained unchanged for CMDBS concns. equal to or higher than 10-5M, whereas CMDBS was found to interfere strongly with the fibrinogen-thrombin interaction. These data suggests that CMDBS has a strong affinity for the protease and no affinity for HC II. The computed dissocn. const. of the CMDBS-thrombin complex (KPS,E) WAS 2.4.times.10-7M and the rate const. of the reaction of this complex with HC II(k) was 1.7.times.109M-1min-1. These findings indicate that CMDBS exerts its catalytic effect through a unique mechanism of action and may constitute a new class of anticoagulant drugs.

L4 ANSWER 2 OF 17 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1996:305575 CAPLUS
DN 125:798
TI A synthetic **dextran derivative** inhibits complement activation and complement-mediated cytotoxicity in an in vitro model of hyperacute xenograft rejection
AU Thomas, H.; Maillet, F.; Letourneur, D.; Jozefonvicz, J.; Kazatchkine, M. D.; Fischer, E.
CS Hopital Broussais, INSERM, Paris, F-75014, Fr.
SO Transplantation Proceedings (1996), 28(2), 593-594
CODEN: TRPPA8; ISSN: 0041-1345
PB Appleton & Lange
DT Journal
LA English
AB A **carboxymethylbenzylamide** sulfonate **dextran**, CMDBS25, bearing 73% carboxylic groups and 15% benzylamide sulfonate groups, is capable of suppressing complement activation at the interface of porcine aortic endothelial cells and normal human serum in an in vitro model of xenogenic rejection.

L4 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1996:155196 CAPLUS
DN 124:220975
TI FGF protection and inhibition of human neutrophil elastase by **carboxymethyl** benzylamide sulfonate **dextran derivatives**
AU Meddahi, Anne; Lemdjabar, Hassan; Caruelle, Jean-Pierre; Barritault, Denis; Hornebeck, William
CS Lab. Recherche Croissance Regeneration Tissulaires, Univ. Paris XII-Val de Marne, Creteil, F94010, Fr.
SO International Journal of Biological Macromolecules (1996), 18(1,2), 141-5
CODEN: IJBMDR; ISSN: 0141-8130
PB Elsevier
DT Journal
LA English
AB Several **derivatized dextrans** (DxD) contg. defined percentage of **carboxymethyl**, **carboxymethyl** benzylamide and **carboxymethyl** benzylamide sulfonate groups have been shown to stimulate tissue repair in various in vivo models including skin, bone, muscle and cornea. These selected DxD were also shown to mimic heparin or heparan sulfate by their ability to interact with, stabilize and protect the heparin-binding growth factor of the fibroblast growth factor family against trypsin digestion. The wound healing action of these DxD was

explained by postulating that the endogenously released heparin-binding growth factors could be protected within the wound. To further understand the action of these DxD on tissue repair, the authors have studied their effect on the human neutrophil elastase (HNE) activity, one of the proteases involved in wound repair. These DxD inhibited HNE in an hyperbolic non-competitive manner. Extent of HNE inhibition by DxD increased with their mol. wt. and benzylamide sulfonate substitution levels. One DxD, RGT11, was the best inhibitor (Ki 40 pM) and efficiently inhibited FGF-2 proteolysis by HNE, restoring its growth-promoting activity towards human skin fibroblasts. The data contribute to a better understanding of the wound-healing property and anti-inflammatory activity of these polymers.

L4 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1996:59901 CAPLUS
DN 124:164792
TI Heparan-like molecules induce the repair of skull defects
AU Blanquaert, F.; Saffar, J. L.; Colombier, M. L.; Carpentier, G.; Barritault, D.; Caruelle, J. P.
CS CNRS, Univ. Paris XII, Creteil, 94010, Fr.
SO Bone (New York) (1995), 17(6), 499-506
CODEN: BONEDL; ISSN: 8756-3282
PB Elsevier
DT Journal
LA English
AB Heparin-binding growth factors (HBGFs) are known to stimulate bone repair when applied to bone lesions. Nevertheless, successful treatments are obtained with high protein doses since HBGFs are rapidly degraded in situ by multiple proteolytic activities assocd. with the inflammatory period of tissue healing. Like heparin or heparan sulfates, heparan-like mols., named **carboxymethyl**-benzylamide-sulfonated **dextrans** (CMDBS), are known to potentiate fibroblast growth factor activities by stabilizing them against pH, thermal or proteolytic denaturations, and by enhancing their binding with cell surface receptors. We have postulated that CMDBS stimulate in vivo bone healing by interacting with endogenous HBGFs, spontaneously released in the wounded site. The effect of CMDBS on bone repair was studied in a skull defect model in rats by computer-assisted radiomorphometry and histomorphometry. Single application of CMDBS in a collagen vehicle to skull defects induced a dose-dependent increase in bone defect closure and new bone formation after 35 days. Complete bony bridging occurred in defects treated with 3 .mu.g CMDBS, whereas bone formation was not obsd. in vehicle-treated defects which contained only dense fibrous connective tissue between the defect margins. These results indicate that heparan-like mols., such as CMDBS, are able to induce bone regeneration of skull defects. This action is possibly mediated by potentiation of endogenous growth factor activities and/or by neutralization of proteolytic activities.

L4 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1995:736640 CAPLUS
DN 123:237721
TI Activation of the complement system by polysaccharide surfaces bearing **carboxymethyl**, **carboxymethylbenzylamide** and **carboxymethylbenzylamide** sulfonate groups
AU Toufik, Jamila; Carreno, Marie-Paule; Jozefowicz, Marcel; Labarre, Denis
CS Lab. Physico-Chimie, Univ. Paris-Sud, Chatenay-Malabry, 92290, Fr.
SO Biomaterials (1995), 16(13), 993-1002
CODEN: BIMADU; ISSN: 0142-9612
PB Elsevier
DT Journal
LA English
AB Substituted Sephadex **derivs**. bearing **carboxymethyl** (CM), CM-benzylamide (CMB), CM-propylamine (CMP) and CMB-sulfonate (CMBS) groups are used as models of polysaccharide surfaces to measure the

effects of substituting OH group on the complement activating capacity (CAC) of the modified surfaces in normal human serum. CM substitution decreases and can suppress the CAC of Sephadex. Low CMB substitution also decreases the CAC, whereas high CMB or CMP substitutions increase it again a min. In addn. to C3 cleavage occurring at high substitution with CMB or CMP groups, the presence of CMB induces consumption of a protein, limiting CH50 measurements. The CAC variations could be due to rearrangements of the polymer surfaces at the aq. interface with proteins. Highly substituted CMB-bearing surfaces could activate complement-like polystyrene surfaces. The presence of CMBS groups does not reduce the CAC of the surface. Such polymer surfaces, which are heparin-like concerning coagulation, are not heparin-like concg. complement inhibition.

L4 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1995:368882 CAPLUS
DN 122:150835
TI **Carboxymethyl** benzylamide **dextrans** inhibit breast cell growth
AU Bagheri-Yarmand, R.; Bittoun, P.; Champion, J.; Letourneur, D.; Jozefonvicz, J.; Fermandjian, S.; Crepin, M.
CS Institut d'Oncologie Cellulaire et Moleculaire Humaine (IOCMH), Bobigny, 93000, Fr.
SO In Vitro Cellular & Developmental Biology: Animal (1994), 30A(12), 822-4
CODEN: IVCAED; ISSN: 1071-2690
DT Journal
LA English
AB Several **dextran derivs**. were investigated to study the influence of substituents on their growth-inhibitory effects with HBL100 and HH9 cell lines. The chem. **derivatization** involved statistical distribution of chem. groups linked to the 1-6 glucosyl units forming the macromol. chains. Results showed that **carboxymethyl** groups linked to glucosyl units and benzylamide groups are required to promote cell growth inhibition.

L4 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1993:400364 CAPLUS
DN 119:364
TI Inhibitory effect of substituted **dextrans** on MCF7 human breast cancer cell growth in vitro
AU Morere, J. F.; Letourneur, D.; Planchon, P.; Avramoglou, T.; Jozefonvicz, J.; Israel, L.; Crepin, M.
CS Serv. Oncol. Med., Hop. Avicenne, Bobigny, 93000, Fr.
SO Anti-Cancer Drugs (1992), 3(6), 629-34
CODEN: ANTDEV; ISSN: 0959-4973
DT Journal
LA English
AB Substituted **dextrans** can reproduce some of the properties of heparin and can thus be used to alter cellular growth. We studied the effect of heparin (H108), **dextran** (D), **carboxymethylbenzylamide dextran** (CMDB) and **carboxymethylbenzylamide** sulfonate **dextran** (CMDBS) on the growth of human mammary cells of the MCF7 tumor line. The cells were cultured in min. Eagle's medium contg. 2% fetal calf serum without biopolymer, or with increasing concns. of H108, D, CMDB or CMDBS. Growth curves were accurately based on cell counting using a Coulter counter. Cell distribution in the various phases of the cycle was analyzed by flow cytometry. Dose-dependent growth inhibitory effects (400-4000 .mu.g/mL) were obsd. The effect on MCF7 tumor cells was most apparent with CMDBS. The percentage of cells in the S phase decreased with preferential blocking in the G0/G1 phase. Pre-clin. studies can be anticipated as there is an absence of in vivo toxicity.

L4 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1992:143841 CAPLUS

DN 116:143841
TI Antitumor **dextran derivatives**
IN Jozefowicz, Jacqueline; Harmand, Marie Francoise; Slaoui, Faouzi
PA Therapeutiques Substitutives, Fr.
SO Fr. Demande, 25 pp.
CODEN: FRXXBL
DT Patent
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	FR 2657782	A1	19910809	FR 1990-1343	19900206
	FR 2657782	B1	19920522		
	CA 2075291	AA	19910807	CA 1991-2075291	19910206
	CA 2075291	C	20020730		
	WO 9112011	A1	19910822	WO 1991-FR92	19910206
	W: CA, JP, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
	EP 514449	A1	19921125	EP 1991-904092	19910206
	EP 514449	B1	19970514		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	JP 05503959	T2	19930624	JP 1991-504244	19910206
	JP 3018046	B2	20000313		
	AT 152912	E	19970515	AT 1991-904092	19910206
	ES 2103799	T3	19971001	ES 1991-904092	19910206
PRAI	FR 1990-1343	A	19900206		
	WO 1991-FR92	W	19910206		

AB An agent for inhibiting tumor cell growth comprises a **carboxymethylated** and **carboxymethylbenzylamide** sulfonated **dextran** DxCMyBSz (D = **dextran**; CMBS = **carboxymethylbenzylamide** sulfonate; x = mean no. saccharide units free/100 saccharide units, .ltoreq. 50; y = mean no. **carboxymethylated** groups/100 saccharide units, 10-90; z = mean no. **carboxymethylbenzylamide** sulfonated groups/100 saccharide units, 15-35). **Dextran deriv**. D11CM60B0S29 at 400 .mu.g/mL in the presence of 5% fetal calf serum inhibited thymidine incorporation by 75% in tumorous chondrocytes.

L4 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1991:687174 CAPLUS
DN 115:287174
TI **Functionalized dextran** and polystyrene as activators of insulin secretion
IN Jozefowicz, Marcel; Jozefowicz, Jacqueline; Serne, Henri; Oturan, Nihal; El Marhoum, Amina
PA Groupement d'Interet Public Therapeutiques Substitutives, Fr.
SO Fr. Demande, 16 pp.
CODEN: FRXXBL
DT Patent
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	FR 2650951	A1	19910222	FR 1989-10964	19890817
PRAI	FR 1989-10964		19890817		

AB Polymers contg. amide or sulfamide groups linked to free alkylamine or arylamine are used as activators of insulin (I) secretion, cell culture supports, and implants. Rats' insulin-secreting cells were cultured on crosslinked **carboxymethylbenzylamine** sulfonate Sephadex and were stimulated by arginine/theophyllline. The amt. of secretion was doubled as compared with non-**functionalized** Sephadex and the rate of the I secretion was relative to the % of **carboxymethylbenzylamide** group.

L4 ANSWER 10 OF 17 IFIPAT COPYRIGHT 2003 IFI on STN
AN 10239575 IFIPAT;IFIUDB;IFICDB
TI PHARMACEUTICAL COMPOSITIONS WITH WOUND HEALING OR ANTI-COMPLEMENTARY ACTIVITY COMPRISING A **DEXTRAN DERIVATIVE**
INF Correia; Jose, Saint Amand les Eaux, FR
Dahricorreia; Latifa, Saint Amand les Eaux, FR
Huynh; Remi, Saint Amand les Eaux, FR
Jozefonvicz; Jacqueline, Lamorlaye, FR
Jozefowicz; Marcel, Lamorlaye, FR
IN Correia Jose (FR); Dahricorreia Latifa (FR); Huynh Remi (FR); Jozefonvicz Jacqueline (FR); Jozefowicz Marcel (FR)
PAF Unassigned
PA Unassigned Or Assigned To Individual (68000)
AG Welsh & Katz, Ltd. Thomas W. Tolpin, 22nd Floor, 120 South Riverside Plaza, Chicago IL, 60606, US
PI US 2002183282 A1 20021205
AI US 2001-20044 20011213
PRAI FR 1999-7636 19990616
WO 2000-FR1658 20000615
FI US 2002183282 20021205
DT Utility; Patent Application - First Publication
FS CHEMICAL
APPLICATION
CLMN 21
GI 3 Figure(s).
FIG. 1 diagrammatically illustrates the structure of a **dextran** which is substituted by the different chemical groups which are attached to the glucoside units; the position of the substituent on the different carbons of the glucoside-based units is shown in position 2, by way of example;
FIG. 2 illustrates the anticomplementary activity of a **dextran derivative** of general formula DMCaBbSuc; in this figure, the CH50 (%), which is measured as indicated in example 5, is depicted in terms of the time (hours);
FIG. 3 shows the healing, after 3 and 7 days (D3 and D7), of dorsal skin incisions which were performed on rats, the wounds being treated either with a physiological solution (photographs in column 1) or with a solution of a **dextran derivative** of general formula DMCaBbSuc (photographs in column 2).
AB The invention concerns pharmaceutical compositions with wound healing or anti-complementary activity, and their uses, said compositions comprising. (1) at least a **dextran derivative** of general formula DMCaBbSuc, a, b, and c respectively representing the degrees of substitution in the groups MC, B and Su, wherein a greater-double-equals 0.6, b=0 or greaterdouble-equals 0.1, and c=0 or ranges widely between 0.1 and 0.5 for a wound healing composition, and a greater-double-equals 0. 3, b greater-double-equals 0.1 and c=0 or ranges widely between 0.1 and 0.4 for a composition with anti-complementary activity; (2) and at least a pharmaceutically acceptable carrier, said **dextran derivative** being present in a single unit dose or at a concentration adapted to the desired wound healing or anticomplementary activity.
CLMN 21 3 Figure(s).
FIG. 1 diagrammatically illustrates the structure of a **dextran** which is substituted by the different chemical groups which are attached to the glucoside units; the position of the substituent on the different carbons of the glucoside-based units is shown in position 2, by way of example;
FIG. 2 illustrates the anticomplementary activity of a **dextran derivative** of general formula DMCaBbSuc; in this figure, the CH50 (%), which is measured as indicated in example 5, is depicted in terms of the time (hours);
FIG. 3 shows the healing, after 3 and 7 days (D3 and D7), of dorsal skin incisions which were performed on rats, the wounds being treated either

with a physiological solution (photographs in column 1) or with a solution of a **dextran derivative** of general formula DMCaBbSuc (photographs in column 2).

L4 ANSWER 11 OF 17 IFIPAT COPYRIGHT 2003 IFI on STN
AN 10225413 IFIPAT;IFIUDB;IFICDB
TI BIOLOGICALLY ACTIVE MATERIAL BASED ON AN INSOLUBILISED **DEXTRAN DERIVATIVE** AND A GROWTH FACTOR
INF Blanchat; Cinderella, Margency, FR
Chaubet; Frederic, Eaubonne, FR
Correia; Jose, Saint Amand Les Eaux, FR
Jozefonvicz; Jacqueline, Lamorlaye, FR
Jozefowicz; Marcel, Lamorlaye, FR
Logeart-Avramoglou; Delphine, Groslay, FR
Meunier; Alain, Saint-Mande, FR
Petite; Herve, Paris, FR
Sedel; Laurent, Jouy en Josas, FR
IN Blanchat Cinderella (FR); Chaubet Frederic (FR); Correia Jose (FR); Jozefonvicz Jacqueline (FR); Jozefowicz Marcel (FR); Logeart-Avramoglou Delphine (FR); Meunier Alain (FR); Petite Herve (FR); Sedel Laurent (FR)
PAF Unassigned
PA Unassigned Or Assigned To Individual (68000)
AG Welsh & Katz, Ltd. Thomas W. Tolpin, 22nd Floor, 120 South Riverside Plaza, Chicago IL, 60606, US
PI US 2002169120 A1 20021114
AI US 2001-16706 20011211
PRAI FR 1999-7401 19990611
WO 2000-FR1603 20000609
FI US 2002169120 20021114
DT Utility; Patent Application - First Publication
FS CHEMICAL
APPLICATION
CLMN 23
GI 7 Figure(s).
FIG. 1 schematically illustrates the structure of a **dextran derivative** of general formula DMCaBbSUcSd;
FIG. 2a represents the results of electrophoreses on 0.8% agarose gel of various polymers and of the growth factor TGFbeta 1;
FIG. 2b represents the results of electrophoreses on 0.8% agarose gel of various polymers and of BMP extracted from a bovine bone tissue;
FIGS. 3a and 3b represent the quantity (in pg, cumulative values) of TGF-beta 1 released by the gels T500 (native **dextran**) and FC27 (substituted **dextran derivative**) as a function of time (in hours), without renewal of the medium (FIG. 3a) and with renewal of the medium (FIG. 3b), respectively, according to the protocol described in example 5;
FIG. 4a represents a radiograph of bone neoformation induced in rats by extracted bovine BMP, according to the protocol described in example 9;
FIG. 4b represents a view under an optical microscope of a bone nodule formed at an intramuscular site in a rat, according to the protocol described in example 9;
FIG. 4c represents a view under an optical microscope of an implant based on coral and extracted bovine BMP at an intramuscular site, in a rat, according to the protocol described in example 9.
AB The invention concerns a biologically active material essentially comprising at least an insolubilised **dextran derivative** of general formula DMCaBbSUcSd and at least a growth factor having an activity on osteoarticular, dental and/or maxillofacial tissues, and the method for preparing same. The invention also concerns the uses of said biomaterial for preparing a repair or filing material, such as an implant, for osteoarticular, dental or maxillofacial applications and for preparing an orthopaedic, dental or maxillofacial prosthesis, and the prosthesis coated with said biologically active material.
CLMN 23 7 Figure(s).

FIG. 1 schematically illustrates the structure of a **dextran derivative** of general formula DMCaBbSUcSd;
FIG. 2a represents the results of electrophoreses on 0.8% agarose gel of various polymers and of the growth factor TGFbeta 1;
FIG. 2b represents the results of electrophoreses on 0.8% agarose gel of various polymers and of BMP extracted from a bovine bone tissue;
FIGS. 3a and 3b represent the quantity (in pg, cumulative values) of TGF-beta 1 released by the gels T500 (native **dextran**) and FC27 (substituted **dextran derivative**) as a function of time (in hours), without renewal of the medium (FIG. 3a) and with renewal of the medium (FIG. 3b), respectively, according to the protocol described in example 5;
FIG. 4a represents a radiograph of bone neoformation induced in rats by extracted bovine BMP, according to the protocol described in example 9;
FIG. 4b represents a view under an optical microscope of a bone nodule formed at an intramuscular site in a rat, according to the protocol described in example 9;
FIG. 4c represents a view under an optical microscope of an implant based on coral and extracted bovine BMP at an intramuscular site, in a rat, according to the protocol described in example 9.

L4 ANSWER 12 OF 17 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
AN 95:537731 SCISEARCH
GA The Genuine Article (R) Number: RM797
TI ACTIVATION OF THE COMPLEMENT-SYSTEM BY POLYSACCHARIDIC SURFACES BEARING **CARBOXYMETHYL**, **CARBOXYMETHYLBENZYLAMIDE** AND **CARBOXYMETHYLBENZYLAMIDE** SULFONATE GROUPS
AU TOUFIK J; CARRENO M P; JOZEFOWICZ M; LABARRE D (Reprint)
CS UNIV PARIS SUD, PHYSICOCHIM LAB, CNRS, URA 1218, F-92290 CHATENAY MALABRY, FRANCE (Reprint); UNIV PARIS SUD, PHYSICOCHIM LAB, CNRS, URA 1218, F-92290 CHATENAY MALABRY, FRANCE; HOP BROUSSAIS, INSERM, U28, IMMUNOPATHOL LAB, F-75014 PARIS, FRANCE; UNIV PARIS SUD, RECH MACROMOLEC LAB, CNRS, URA 502, F-93430 VILLETANEUSE, FRANCE
CYA FRANCE
SO BIOMATERIALS, (SEP 1995) Vol. 16, No. 13, pp. 993-1002.
ISSN: 0142-9612.
DT Article; Journal
FS LIFE
LA ENGLISH
REC Reference Count: 27
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Substituted Sephadex (R) **derivatives** bearing **carboxymethyl** (CM), CM-benzylamide (CMB), CM-propylamide (CMP) and CMB-sulphonate (CMBS) groups are used as models of polysaccharidic surfaces to measure the effects of substituting OH groups on the complement activating capacity (CAC) of the modified surfaces in normal human serum. CM substitution decreases and can suppress the CAC of Sephadex. Low CMB substitution also decreases the CAC, whereas high CMB or CMP substitutions increase it again after a minimum. In addition to C3 cleavage occurring at high substitution with CMB or CMP groups, the presence of CMB induces consumption of a protein, limiting CH50 measurements. The CAC variations could be due to rearrangements of the polymer surfaces at the aqueous interface with proteins. Highly substituted CMB-bearing surfaces could activate complement-like polystyrene surfaces. The presence of CMBS groups does not reduce the CAC of the surface. Such polymer surfaces, which are heparin-like concerning coagulation, are not heparin-like concerning complement inhibition.

L4 ANSWER 13 OF 17 USPATFULL on STN
AN 2002:323116 USPATFULL
TI Pharmaceutical compositions with wound healing or anti-complementary activity comprising a **dextran derivative**
IN Dahricorreia, Latifa, Saint Amand les Eaux, FRANCE
Jozefonvicz, Jacqueline, Lamorlaye, FRANCE

Jozefowicz, Marcel, Lamorlaye, FRANCE
Correia, Jose, Saint Amand les Eaux, FRANCE
Huynh, Remi, Saint Amand les Eaux, FRANCE
PI US 2002183282 A1 20021205
AI US 2001-20044 A1 20011213 (10)
PRAI FR 1999-7636 19990616
WO 2000-FR1658 20000615
DT Utility
FS APPLICATION
LREP Welsh & Katz, Ltd., Thomas W. Tolpin, 22nd Floor, 120 South Riverside Plaza, Chicago, IL, 60606
CLMN Number of Claims: 21
ECL Exemplary Claim: 1
DRWN 3 Drawing Page(s)
LN.CNT 929
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention concerns pharmaceutical compositions with wound healing or anti-complementary activity, and their uses, said compositions comprising. (1) at least a **dextran derivative** of general formula DMC.sub.aB.sub.bSu.sub.c, a, b, and c respectively representing the degrees of substitution in the groups MC, B and Su, wherein a .gtoreq.0.6, b=0 or .gtoreq.0.1, and c=0 or ranges widely between 0.1 and 0.5 for a wound healing composition, and a.gtoreq.0.3, b .gtoreq.0.1 and c=0 or ranges widely between 0.1 and 0.4 for a composition with anti-complementary activity; (2) and at least a pharmaceutically acceptable carrier, said **dextran derivative** being present in a single unit dose or at a concentration adapted to the desired wound healing or anti-complementary activity.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 14 OF 17 USPATFULL on STN
AN 2002:301575 USPATFULL
TI Biologically active material based on an insolubilised **dextran derivative** and a growth factor
IN Blanchat, Cinderella, Margency, FRANCE
Logeart-Avramoglou, Delphine, Groslay, FRANCE
Petite, Herve, Paris, FRANCE
Meunier, Alain, Saint-Mande, FRANCE
Chaubet, Frederic, Eaubonne, FRANCE
Jozefonvicz, Jacqueline, Lamorlaye, FRANCE
Jozefowicz, Marcel, Lamorlaye, FRANCE
Sedel, Laurent, Jouy en Josas, FRANCE
Correia, Jose, Saint Amand Les Eaux, FRANCE
PI US 2002169120 A1 20021114
AI US 2001-16706 A1 20011211 (10)
PRAI FR 1999-7401 19990611
WO 2000-FR1603 20000609
DT Utility
FS APPLICATION
LREP Welsh & Katz, Ltd., Thomas W. Tolpin, 22nd Floor, 120 South Riverside Plaza, Chicago, IL, 60606
CLMN Number of Claims: 23
ECL Exemplary Claim: 1
DRWN 4 Drawing Page(s)
LN.CNT 983
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention concerns a biologically active material essentially comprising at least an insolubilised **dextran derivative** of general formula DMC.sub.aB.sub.bSU.sub.cS.sub.d and at least a growth factor having an activity on osteoarticular, dental and/or maxillofacial tissues, and the method for preparing same. The invention also concerns the uses of said biomaterial for preparing a

repair or filing material, such as an implant, for osteoarticular, dental or maxillofacial applications and for preparing an orthopaedic, dental or maxillofacial prosthesis, and the prosthesis coated with said biologically active material.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 15 OF 17 WPINDEX COPYRIGHT 2003 THOMSON DERWENT on STN
AN 1999-385580 [32] WPINDEX
DNC C1999-113486
TI New **dextran derivatives** with anticoagulant and antithrombotic activity.
DC B04
IN CHAUBET, F; CORREIA, J; DAHRI, L; HUYNH, R; JOZEFOWICZ, J; JOZEFOWICZ, M; JOZEFONVICZ, J
PA (SOLU-N) SOLUTIONS SA; (SOLU-N) SOLUTIONS
CYC 77
PI WO 9929734 A1 19990617 (199932)* FR 46p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AU BA BB BG BR CA CN CU CZ EE GD GE HR HU ID IL IN IS JP KG KP KR LC LK LR LT LV MG MK MN MX NO NZ PL RO SG SI SK SL TR TT UA US UZ VN YU ZW
FR 2772382 A1 19990618 (199932)
AU 9915677 A 19990628 (199946)
EP 990002 A1 20000405 (200021) FR
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
JP 2001523300 W 20011120 (200204) 49p
ADT WO 9929734 A1 WO 1998-FR2699 19981211; FR 2772382 A1 FR 1997-15702 19971211; AU 9915677 A AU 1999-15677 19981211; EP 990002 A1 EP 1998-959962 19981211, WO 1998-FR2699 19981211; JP 2001523300 W WO 1998-FR2699 19981211, JP 1999-530262 19981211
FDT AU 9915677 A Based on WO 9929734; EP 990002 A1 Based on WO 9929734; JP 2001523300 W Based on WO 9929734
PRAI FR 1997-15702 19971211
AN 1999-385580 [32] WPINDEX
AB WO 9929734 A UPAB: 19990813
NOVELTY - New **derivatives** of **dextran** (I) which have medical use with specific biological action.
DETAILED DESCRIPTION - **Dextran derivatives** of formula DMCaBbSucSd (I) are new.
D = polysaccharide chain, preferably formed by chains of glucoside units;
MC = methylcarboxylate groups;
B = **carboxymethylbenzylamide** groups;
Su = sulphate groups;
S = sulphonate groups;
a-d = degree of substitution (ds), in groups MC, B, Su and S respectively, expressed as the ratio to the number of free hydroxyl groups in the glucoside unit of the **dextran**;
a = 0 or is greater than or equal to 0.3;
b = 0 or is greater than or equal to 0.1;
c = 0 or greater than or equal to 0.1;
d = 0 or less than or equal to 0.15;
provided that when d = 0, then a and/or b are not zero.
(I) have homogeneity in:
(a) the distribution of chain size illustrated by a gaussian elution profile symmetrical in high performance steric exclusion chromatography;
(b) the distribution of charged chemical groups illustrated by an elution profile with a single symmetrical peak in low pressure ion-exchange chromatography.
INDEPENDENT CLAIMS are also included for:
(1) medicaments comprising (I) as active agent, optionally with another active agent and/or at least one active agent vehicle and/or a

support, preferably a liposome;
(2) the preparation of (I);
(3) **dextran carboxymethyl** benzylamide of formula DMCaBb (II) where a and b are both other than 0, as intermediate for (I); and
(4) **dextran** benzylamide as intermediate for (I).
ACTIVITY - Cicatrizant; anticoagulant; anti-complementary agent.
Anticoagulant activity was measured using the time of activity of cephalin. DMCBSu1 had anticoagulant activity of 0.02 IU/mg compared to 4.0 IU/mg for DMCBSu3 and 173 IU/mg for heparin.
MECHANISM OF ACTION - None given.
USE - (II) is useful as an agent with anti-complementary activity (claimed). (I) are useful as plasma substitutes and for modulating cellular proliferation.
The following uses are claimed:
(1) (I) in which a is greater than or equal to 0.6, b is not zero, c is 0 or less than or equal to 0.5, and d is less than or equal to 0.15 or 0 and the molar mass is 3000 -500 000 g/mole, are useful as cicatrizants;
(2) (I) in which a is greater than or equal to 0.3, b is not 0, c is 0 or less than or equal to 0.4, and d is less than or equal to 0.15 or 0, with a molar mass of 10000-60000 g/mole have anti-complementary activity and are plasma substitutes;
(3) (I) in which a is greater than or equal to 0.5, b is not 0, c is 0 or less than or equal to 0.4, d is less than or equal to 0.15 or 0 and the molar mass is 3000-100000 g/mole, are for modulating cellular proliferation;
(4) (I) in which a is greater than or equal to 0.4, b is not 0, c is greater than or equal to 0.3 and d is less than or equal to 0.15 or 0, with a molar mass of 3000-20000 g/mole, are useful as anticoagulants.
ADVANTAGE - The process enables the degree of substitution of the dextran, the homogeneity of the distribution of chemical groups and the homogeneity of the size of the polysaccharide chains of the product to be controlled, giving improved reproducibility. The process uses less steps than in the prior art and gives improved yields, e.g. 80% for stages (a) and (b) and 60% for stage (c).
Dwg.1/3

L4 ANSWER 16 OF 17 WPINDEX COPYRIGHT 2003 THOMSON DERWENT on STN
AN 1991-266893 [36] WPINDEX
DNC C1991-115673
TI New antitumour agent derived from **dextran** - comprises polysaccharide chain with **carboxymethyl** and **carboxymethyl** benzyl amide sulphonate gps..
DC A96 B04 D16
IN HARMAND, M; JOZEFOWICZ, J; SLAQUI, F; SLAOUI, F; HARMAND, M F
PA (THER-N) THERAPEUTIQUES SUBSTITUTIVES; (THER-N) THERAPEUTIQUES SUBS
CYC 17
PI WO 9112011 A 19910822 (199136)* 27p
RW: AT BE CH DE DK ES FR GB GR IT LU NL SE
W: CA JP US
FR 2657782 A 19910809 (199144)
EP 514449 A1 19921125 (199248) FR 27p
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE
JP 05503959 W 19930624 (199330) 10p
EP 514449 B1 19970514 (199724) FR 16p
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE
DE 69126129 E 19970619 (199730)
ES 2103799 T3 19971001 (199746)
JP 3018046 B2 20000313 (200017) 13p
CA 2075291 C 20020730 (200259) FR
ADT FR 2657782 A FR 1990-1343 19900206; EP 514449 A1 EP 1991-904092 19910206, WO 1991-FR92 19910206; JP 05503959 W JP 1991-504244 19910206, WO 1991-FR92 19910206; EP 514449 B1 EP 1991-904092 19910206, WO 1991-FR92 19910206; DE 69126129 E DE 1991-626129 19910206, EP 1991-904092 19910206, WO 1991-FR92

19910206; ES 2103799 T3 EP 1991-904092 19910206; JP 3018046 B2 JP 1991-504244 19910206, WO 1991-FR92 19910206; CA 2075291 C CA 1991-2075291 19910206, WO 1991-FR92 19910206

FDT EP 514449 A1 Based on WO 9112011; JP 05503959 W Based on WO 9112011; EP 514449 B1 Based on WO 9112011; DE 69126129 E Based on EP 514449, Based on WO 9112011; ES 2103799 T3 Based on EP 514449; JP 3018046 B2 Previous Publ. JP 05503959, Based on WO 9112011; CA 2075291 C Based on WO 9112011

PRAI FR 1990-1343 19900206

AN 1991-266893 [36] WPINDEX

AB WO 9112011 A UPAB: 19930928
Agents for inhibiting tumour cell growth comprises a **dextran deriv**. consisting of a polysaccharide substd. by **carboxymethyl** (CM) and **carboxymethylbenzylamide** sulphonate (CMBS), the **deriv**. being of formula DxCMYBSZ. X = averge number of unsubstd. saccharide units per 100 saccharide units. Y = average number of CM gps. per 100 saccharide units. Z = average no. of CMBS gps. per 100 saccharide units provided that when X is at least 50, Y = 10-90 and Z = 15-35.

USE/ADVANTAGE - (I) are nontoxic and are active against a wise range of tumours.

In an example, at a dose of 200 alphag/ml D11CM60BOS29 gives 75% inhibition of thymidine uptake, and proliferation of human chondrocarcoma (II) cells is totally inhibited. This inhibition is reversible.
0/8

ABEQ JP 05503959 W UPAB: 19931118
Agents for inhibiting tumour cell growth comprises a **dextran deriv**. consisting of a polysaccharide substd. by **carboxymethyl** (CM) and **carboxymethylbenzylamide** sulphonate (CMBS), the **deriv**. being of formula DXCMYBSZ. X = average number of unsubstd. saccharide units per 100 saccharide units. Y = average number of CM gps. per 100 saccharide units. Z = average no. of CMBS gps. per 100 saccharide units provided that when X is at least 50, Y = 10-90 and Z = 15-35.

USE/ADVANTAGE - (I) are non-toxic and are active against a wide range of tumours.

In an example, D11CM60BOS29 at a dose of 200 alphag/ml gives 75% inhibition of thymidine uptake, and proliferation of human chondrocarcoma (II) cells is totally inhibited. This inhibition is reversible.

ABEQ EP 514449 B UPAB: 19970612
Use of a dextrane **derivative** constituted by a polysaccharide chain substituted by **carboxymethyl** and **carboxymethyl** benzyl amide sulphonate groups, the said **derivative** being designated by the general formula DXCMYBSZ in which X represents the average number of non-substituted saccharide units per 100 saccharide units, Y represents the average number of **carboxymethyl** groups per 100 saccharide units, Z represents the average number of **carboxymethyl** benzyl amide sulphonate groups per 100 saccharide groups and X is less than or equal to 50, Y is comprised between 10 and 90 and Z is comprised between 15 and 35 in order to obtain an agent inhibiting the growht of tumoral cells.
Dwg.0/8

L4 ANSWER 17 OF 17 WPINDEX COPYRIGHT 2003 THOMSON DERWENT on STN

AN 1988-021567 [03] WPINDEX

DNC C1988-009502

TI New protein fraction with co-factor activity for growth factors - isolated from crude growth factor by affinity chromatography, useful e.g. in culture media.

DC A96 B04 D16

IN COURTOIS, Y G; GULINO, D; JOSEFOWICZ, M; JOZEFONVIC, J; LENFANT, M; UHLRICH, S M

PA (CNRS) CNRS CENT NAT RECH SCI; (COUR-I) COURTOIS Y G C

CYC 15

PI WO 8800207 A 19880114 (198803)* FR 31p

W: JP US
EP 254616 A 19880127 (198804) FR
R: AT BE CH DE ES FR GB GR IT LI LU NL SE
FR 2600655 A 19871231 (198808)
JP 01500352 W 19890209 (198912)
ADT WO 8800207 A WO 1987-700253 19870630; EP 254616 A EP 1987-401509 19870630; FR 2600655 A FR 1986-9476 19860630; JP 01500352 W JP 1987-503923 19870630
PRAI FR 1986-9476 19860630
AN 1988-021567 [03] WPINDEX
AB WO 8800207 A UPAB: 19930923
A protein fraction (A) having at least partial co-factor activity for growth factor (GF) comprises purifying GF by affinity chromatography on (1) resin I having heparin fixed to a polysaccharide support and/or (2) resin II consisting of crosslinked **dextran**, having **carboxymethyl**, **carboxymethylbenzyl** amide-sulphonate and opt. also **carboxymethylbenzylamide functional** gps., and having biological properties similar to heparin.

When resin I is used, elution is with a neutral buffer having ionic strength approx. equal to that of NACL, and when resin II is used, elution is with a neutral buffer having ionic strength approx. equal to 2 M NaCl.

USE/ADVANTAGE - (A) and its sub-fractions, stimulate and potentiate GF so are useful in cell culture media; in cicatrisation of the skin and cornea; to improve nerve cell survival; to control vascularisation; and as an angiogenesis co-factor in cosmetics for topical application to skin and hair.

0/10

=> dis hist

(FILE 'HOME' ENTERED AT 11:43:17 ON 24 JUL 2003)

FILE 'APOLLIT, BABS, CAPLUS, CBNB, CEN, CIN, EMA, IFIPAT, JICST-EPLUS, PASCAL, PLASNEWS, PROMT, RAPRA, SCISEARCH, TEXTILETECH, USPATFULL, USPAT2, WPINDEX, WTEXTILES' ENTERED AT 11:43:31 ON 24 JUL 2003

L1 108349 S DEXTRAN
L2 45437 S L1 AND (DERIVAT? OR FUNCTIONAL?)
L3 13447 S L2 AND (METHYLCARBOXYL OR CARBOXYMETHYL?)
L4 17 S L3 AND CARBOXYMETHYLBENZYLAMIDE
L5 8 S L4 AND (SULFAT? OR SULPHAT?)

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PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	Feb 24	PCTGEN now available on STN
NEWS 4	Feb 24	TEMA now available on STN
NEWS 5	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS 6	Feb 26	PCTFULL now contains images
NEWS 7	Mar 04	SDI PACKAGE for monthly delivery of multifile SDI results
NEWS 8	Mar 24	PATDPAFULL now available on STN
NEWS 9	Mar 24	Additional information for trade-named substances without structures available in REGISTRY
NEWS 10	Apr 11	Display formats in DGENE enhanced
NEWS 11	Apr 14	MEDLINE Reload
NEWS 12	Apr 17	Polymer searching in REGISTRY enhanced
NEWS 13	Jun 13	Indexing from 1947 to 1956 added to records in CA/CAPLUS
NEWS 14	Apr 21	New current-awareness alert (SDI) frequency in WPIDS/WPINDEX/WPIX
NEWS 15	Apr 28	RDISCLOSURE now available on STN
NEWS 16	May 05	Pharmacokinetic information and systematic chemical names added to PHAR
NEWS 17	May 15	MEDLINE file segment of TOXCENTER reloaded
NEWS 18	May 15	Supporter information for ENCOMPPAT and ENCOMPLIT updated
NEWS 19	May 19	Simultaneous left and right truncation added to WSCA
NEWS 20	May 19	RAPRA enhanced with new search field, simultaneous left and right truncation
NEWS 21	Jun 06	Simultaneous left and right truncation added to CBNB
NEWS 22	Jun 06	PASCAL enhanced with additional data
NEWS 23	Jun 20	2003 edition of the FSTA Thesaurus is now available
NEWS 24	Jun 25	HSDB has been reloaded
NEWS 25	Jul 16	Data from 1960-1976 added to RDISCLOSURE
NEWS 26	Jul 21	Identification of STN records implemented
NEWS 27	Jul 21	Polymer class term count added to REGISTRY
NEWS 28	Jul 22	INPADOC: Basic index (/BI) enhanced; Simultaneous Left and Right Truncation available

NEWS EXPRESS	April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP), AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

* * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

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FILE 'HOME' ENTERED AT 11:53:34 ON 24 JUL 2003

=>  caplus
CAPLUS IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s DAHRICORREIA L?/AU
THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE
Some commands only work in certain files.  For example, the EXPAND
command can only be used to look at the index in a file which has an
index.  Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of
commands which can be used in this file.

=> FILE CAPLUS
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     1.05       1.05

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FILE COVERS 1907 - 24 Jul 2003  VOL 139 ISS 4
FILE LAST UPDATED: 23 Jul 2003  (20030723/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.


=> s DAHRICORREIA L?/AU
L1            0 DAHRICORREIA L?/AU

=> S JOZEFONVICZ J?/AU
L2          178 JOZEFONVICZ J?/AU

=> S JOZEFOWICZ M?/AU
L3          189 JOZEFOWICZ M?/AU

=> S CORREIA J?/AU
L4          291 CORREIA J?/AU

=> S HUYNH R?/AU
L5            9 HUYNH R?/AU

=> S L1 AND L2 AND L3 AND L4 AND L5 AND DEXTRAN
         30600 DEXTRAN
          3912 DEXTRANS
         31331 DEXTRAN
                 (DEXTRAN OR DEXTRANS)
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=>  S L1 AND L2 AND L3 AND L4 AND L5 AND (DEXTRAN OR CMDBS OR DMCBSu)
         30600 DEXTRAN
          3912 DEXTRANS
         31331 DEXTRAN
                 (DEXTRAN OR DEXTRANS)
            26 CMDBS
             1 DMCBSU
L7            0 L1 AND L2 AND L3 AND L4 AND L5 AND (DEXTRAN OR CMDBS OR DMCBSU)

=>  S L2 AND L3 AND L4 AND L5 AND DEXTRAN
         30600 DEXTRAN
          3912 DEXTRANS
         31331 DEXTRAN
                 (DEXTRAN OR DEXTRANS)
L8            2 L2 AND L3 AND L4 AND L5 AND DEXTRAN

=> dis l8 1-2 bib abs

L8   ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2003 ACS on STN
AN   2000:900400  CAPLUS
DN   134:46808
TI   Pharmaceutical compositions with wound healing or anti-complementary
     activity comprising a dextran derivative
IN   Dahri-correia, Latifa; Jozefonvicz, Jacqueline; Jozefowicz,
     Marcel; Correia, Jose; Huynh, Remi
PA   Iterfi, Fr.
SO   PCT Int. Appl., 26 pp.
     CODEN: PIXXD2
DT   Patent
LA   French
FAN.CNT 1
     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ---------------   ----  --------      ---------------  --------
PI   WO 2000076452     A2    20001221      WO 2000-FR1658   20000615
     WO 2000076452     A3    20010809
         W:  CA, JP, US
         RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE
     FR 2794976        A1    20001222      FR 1999-7636     19990616
     JP 2003501449     T2    20030114      JP 2001-502792   20000615
     US 2002183282     A1    20021205      US 2001-20044    20011213
PRAI FR 1999-7636      A     19990616
     WO 2000-FR1658    W     20000615
AB   The invention concerns pharmaceutical compns. with wound healing or
     anti-complementary activity, and their uses, said compns. comprising. (1)
     at least a dextran deriv. of general formula DMCaBbSuc, a, b,
     and c resp. representing the degrees of substitution in the groups MC, B
     and Su, wherein a <<geq 0.6, b = 0 or <<geq 0.1, and c = 0 or ranges
     widely between 0.1 and 0.5 for a wound healing compn., and a <<geq 0.3, b
     <<geq 0.1 and c = 0 or ranges widely between 0.1 and 0.4 for a compn. with
     anti-complementary activity; (2) and at least a pharmaceutically
     acceptable carrier, said dextran deriv. being present in a
     single unit dose or at a concn. adapted to the desired wound healing or
     anti-complementary activity.  Desulfated dextrans contg. 0.43 g
     sulfur per 100 g were prepd. (prepn. given).  Efficacy of a soln. of 50
     .mu.g/mL desulfated dextran in the cutaneous wound healing of
     rabbits was shown.

L8   ANSWER 2 OF 2  CAPLUS  COPYRIGHT 2003 ACS on STN
AN   1999:388197  CAPLUS
DN   131:46287
TI   Dextran derivatives, their preparation and medical applications
```

with specific biological action
IN Chaubet, Frederic; **Huynh, Remi**; Dahri, Latifa; **Correia, Jose**; **Jozefowicz, Marcel**; **Jozefonvicz, Jacqueline**
PA Solutions, Fr.
SO PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9929734	A1	19990617	WO 1998-FR2699	19981211
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2772382	A1	19990618	FR 1997-15702	19971211
FR 2772382	B1	20000303		
AU 9915677	A1	19990628	AU 1999-15677	19981211
EP 990002	A1	20000405	EP 1998-959962	19981211
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001523300	T2	20011120	JP 1999-530262	19981211
PRAI FR 1997-15702	A	19971211		
WO 1998-FR2699	W	19981211		

AB The derivs. correspond to the general formula DMCaBbSucSd (I), in which D represents a polysaccharide chain, preferably consisting of sequences of glucoside units, MC represents CH2CO2Na ether groups, B represents CH2CONHCH2Ph ether groups, Su represents Na sulfate groups, S represents sulfonate groups (esp. CH2CONHCH2C6H4SO3Na-p ethers), a, b, c and d represent the degree of substitution (d.s.) for groups MC, B, Su and S, resp.; a being 0 or .gtoreq.0.3, b and c being 0 or .gtoreq.0.1, and d being 0-0.15, provided that when d = 0, a and/or b are not 0, the products having a homogeneous chain-size distribution, evidenced by a sym. Gaussian elution profile in high-performance steric exclusion chromatog., and a homogeneous distribution of charged chem. groups, evidenced by an elution profile with a single sym. peak in low-pressure ion-exchange chromatog. Thus, successive carboxymethylation, benzylamidation, and sulfation (with pyridine-SO3 in DMSO) of **dextran** T 40 gave I (a = 0.75, b = 0.20, c = 0.15, d = 0) with mol. wt. 48,000, useful as a plasma substitute. Similarly, I (a = 1.00, c = 0.37, b = d = 0) with mol. wt. 70,000 showed anticoagulant activity.
RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> S L3 AND L4 AND L5 AND DEXTRAN
30600 DEXTRAN
3912 DEXTRANS
31331 DEXTRAN
(DEXTRAN OR DEXTRANS)
L9 2 L3 AND L4 AND L5 AND DEXTRAN

=> dis l9 1-2 bib abs

L9 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:900400 CAPLUS
DN 134:46808
TI Pharmaceutical compositions with wound healing or anti-complementary activity comprising a **dextran** derivative
IN Dahri-correia, Latifa; Jozefonvicz, Jacqueline; **Jozefowicz, Marcel**

; **Correia, Jose**; **Huynh, Remi**
PA Iterfi, Fr.
SO PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000076452	A2	20001221	WO 2000-FR1658	20000615
	WO 2000076452	A3	20010809		
	W: CA, JP, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	FR 2794976	A1	20001222	FR 1999-7636	19990616
	JP 2003501449	T2	20030114	JP 2001-502792	20000615
	US 2002183282	A1	20021205	US 2001-20044	20011213
PRAI	FR 1999-7636	A	19990616		
	WO 2000-FR1658	W	20000615		

AB The invention concerns pharmaceutical compns. with wound healing or anti-complementary activity, and their uses, said compns. comprising. (1) at least a **dextran** deriv. of general formula DMCaBbSuc, a, b, and c resp. representing the degrees of substitution in the groups MC, B and Su, wherein a <<geq 0.6, b = 0 or <<geq 0.1, and c = 0 or ranges widely between 0.1 and 0.5 for a wound healing compn., and a <<geq 0.3, b <<geq 0.1 and c = 0 or ranges widely between 0.1 and 0.4 for a compn. with anti-complementary activity; (2) and at least a pharmaceutically acceptable carrier, said **dextran** deriv. being present in a single unit dose or at a concn. adapted to the desired wound healing or anti-complementary activity. Desulfated **dextrans** contg. 0.43 g sulfur per 100 g were prepd. (prepn. given). Efficacy of a soln. of 50 .mu.g/mL desulfated **dextran** in the cutaneous wound healing of rabbits was shown.

L9 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:388197 CAPLUS
DN 131:46287
TI **Dextran** derivatives, their preparation and medical applications with specific biological action
IN Chaubet, Frederic; **Huynh, Remi**; Dahri, Latifa; **Correia, Jose**; **Jozefowicz, Marcel**; Jozefonvicz, Jacqueline
PA Solutions, Fr.
SO PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9929734	A1	19990617	WO 1998-FR2699	19981211
	W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	FR 2772382	A1	19990618	FR 1997-15702	19971211
	FR 2772382	B1	20000303		
	AU 9915677	A1	19990628	AU 1999-15677	19981211
	EP 990002	A1	20000405	EP 1998-959962	19981211
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2001523300	T2	20011120	JP 1999-530262	19981211

PRAI FR 1997-15702 A 19971211
WO 1998-FR2699 W 19981211
AB The derivs. correspond to the general formula DMCaBbSucSd (I), in which D represents a polysaccharide chain, preferably consisting of sequences of glucoside units, MC represents CH2CO2Na ether groups, B represents CH2CONHCH2Ph ether groups, Su represents Na sulfate groups, S represents sulfonate groups (esp. CH2CONHCH2C6H4SO3Na-p ethers), a, b, c and d represent the degree of substitution (d.s.) for groups MC, B, Su and S, resp.; a being 0 or .gtoreq.0.3, b and c being 0 or .gtoreq.0.1, and d being 0-0.15, provided that when d = 0, a and/or b are not 0, the products having a homogeneous chain-size distribution, evidenced by a sym. Gaussian elution profile in high-performance steric exclusion chromatog., and a homogeneous distribution of charged chem. groups, evidenced by an elution profile with a single sym. peak in low-pressure ion-exchange chromatog. Thus, successive carboxymethylation, benzylamidation, and sulfation (with pyridine-SO3 in DMSO) of **dextran** T 40 gave I (a = 0.75, b = 0.20, c = 0.15, d = 0) with mol. wt. 48,000, useful as a plasma substitute. Similarly, I (a = 1.00, c = 0.37, b = d = 0) with mol. wt. 70,000 showed anticoagulant activity.
RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s l2 and dextran
30600 DEXTRAN
3912 DEXTRANS
31331 DEXTRAN
(DEXTRAN OR DEXTRANS)
L10 90 L2 AND DEXTRAN

=> s l10 and carboxymethylbenzylamide
10 CARBOXYMETHYLBENZYLAMIDE
L11 4 L10 AND CARBOXYMETHYLBENZYLAMIDE

=> dis l11 1-4 bib bas
'BAS' IS NOT A VALID FORMAT FOR FILE 'CAPLUS'

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ABS --------- GI and AB
ALL --------- BIB, AB, IND, RE
APPS -------- AI, PRAI
BIB --------- AN, plus Bibliographic Data and PI table (default)
CAN --------- List of CA abstract numbers without answer numbers
CBIB -------- AN, plus Compressed Bibliographic Data
DALL -------- ALL, delimited (end of each field identified)
DMAX -------- MAX, delimited for post-processing
FAM --------- AN, PI and PRAI in table, plus Patent Family data
FBIB -------- AN, BIB, plus Patent FAM
IND --------- Indexing data
IPC --------- International Patent Classifications
MAX --------- ALL, plus Patent FAM, RE
PATS -------- PI, SO
SAM --------- CC, SX, TI, ST, IT
SCAN -------- CC, SX, TI, ST, IT (random display, no answer numbers; SCAN must be entered on the same line as the DISPLAY, e.g., D SCAN or DISPLAY SCAN)
STD --------- BIB, IPC, and NCL

IABS -------- ABS, indented with text labels
IALL -------- ALL, indented with text labels
IBIB -------- BIB, indented with text labels
IMAX -------- MAX, indented with text labels
ISTD -------- STD, indented with text labels

OBIB -------- AN, plus Bibliographic Data (original)
OIBIB ------- OBIB, indented with text labels

SBIB -------- BIB, no citations
SIBIB ------- IBIB, no citations

HIT --------- Fields containing hit terms
HITIND ------ IC, ICA, ICI, NCL, CC and index field (ST and IT) containing hit terms
HITRN ------- HIT RN and its text modification
HITSTR ------ HIT RN, its text modification, its CA index name, and its structure diagram
HITSEQ ------ HIT RN, its text modification, its CA index name, its structure diagram, plus NTE and SEQ fields
FHITSTR ----- First HIT RN, its text modification, its CA index name, and its structure diagram
FHITSEQ ----- First HIT RN, its text modification, its CA index name, its structure diagram, plus NTE and SEQ fields
KWIC -------- Hit term plus 20 words on either side
OCC --------- Number of occurrence of hit term and field in which it occurs

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All of the formats (except for SAM, SCAN, HIT, HITIND, HITRN, HITSTR, FHITSTR, HITSEQ, FHITSEQ, KWIC, and OCC) may be used with DISPLAY ACC to view a specified Accession Number.
ENTER DISPLAY FORMAT (BIB):end

=> dis l11 1-4 bib abs

L11 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1997:108422 CAPLUS
DN 126:220468
TI Mechanism of thrombin inhibition by heparin cofactor II in the presence of dermatan sulfates, native or oversulfated, and a heparin-like **dextran** derivative
AU Maaroufi, Raoui M.; Jozefowicz, Marcel; Tapon-Bretaudiere, Tapon; **Jozefonvicz, Jacqueline**; Fischer, Anne-Marie
CS Lab. Hematolgie, CHU Necker-Enfants Malades, Paris, 75743, Fr.
SO Biomaterials (1997), 18(4), 359-366
CODEN: BIMADU; ISSN: 0142-9612
PB Elsevier
DT Journal
LA English
AB The kinetics of thrombin inhibition by heparin cofactor II (HC II) in the presence of dermatan sulfatees, native (DS), or oversulfated (DSS 1 and DSS 2) and a biospecific **dextran** deriv. substituted with carboxymethyl, carboxymethyl-benzylamide and carboxymethyl benzylamide-sulfonate functional groups (CMDBS), has been studied as a function of the sulfated polysaccharide concn. The initial HC II and thrombin concns. were set at equimolar levels. Anal. of the exptl. data obtained for DS, DSS1 and DSS2 was performed using a previously described model which allows computation of the dissocn. const. (KPS,HC) of the polysaccharide-HC II complex and the rate const. of thrombin inhibition by the polysaccharide-HC II complex (k). A KPS,HC of 9.6.times.10-7M and a k of 4.5.times.109M-1 were found for DS, whereas KPS,HC 2.1.times.10-6M, k 1.1.times.1010M-1min-1 and KPS,HC 4.3.times.10-7M, k 1.4.times.1010M-1min-1 were found for DSS1 and DSS2, resp. Knowing that DSS1 has a sulfur

content per disaccharide of 7.8%, compared with 11.5% for DDS2, these results indicate that the polysaccharide affinity for HC II is increased only in the case of DSS 2, whereas the oversulfation increases the reactivities towards thrombin of both complexes DSS1-HC II and DSS2-HC II. A better conformation of these complexes may favor a faster interaction with the protease. Unlike heparin, DS at concns. higher than 10-5M does not modify the reaction rate of thrombin inhibition, a fact which can be explained by the absence of complex formation between DS and thrombin. The exptl. data obtained for CMDBS fit a kinetic model in which the biospecific **dextran** deriv. rapidly forms a complex with thrombin which is more reactive towards HC II than the free protease. The reaction rate remained unchanged for CMDBS concns. equal to or higher than 10-5M, whereas CMDBS was found to interfere strongly with the fibrinogen-thrombin interaction. These data suggests that CMDBS has a strong affinity for the protease and no affinity for HC II. The computed dissocn. const. of the CMDBS-thrombin complex (KPS,E) WAS 2.4.times.10-7M and the rate const. of the reaction of this complex with HC II(k) was 1.7.times.109M-1min-1. These findings indicate that CMDBS exerts its catalytic effect through a unique mechanism of action and may constitute a new class of anticoagulant drugs.

L11 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1996:305575 CAPLUS
DN 125:798
TI A synthetic **dextran** derivative inhibits complement activation and complement-mediated cytotoxicity in an in vitro model of hyperacute xenograft rejection
AU Thomas, H.; Maillet, F.; Letourneur, D.; **Jozefonvicz, J.**; Kazatchkine, M. D.; Fischer, E.
CS Hopital Broussais, INSERM, Paris, F-75014, Fr.
SO Transplantation Proceedings (1996), 28(2), 593-594
CODEN: TRPPA8; ISSN: 0041-1345
PB Appleton & Lange
DT Journal
LA English
AB A **carboxymethylbenzylamide** sulfonate **dextran**, CMDBS25, bearing 73% carboxylic groups and 15% benzylamide sulfonate groups, is capable of suppressing complement activation at the interface of porcine aortic endothelial cells and normal human serum in an in vitro model of xenogenic rejection.

L11 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1995:368882 CAPLUS
DN 122:150835
TI Carboxymethyl benzylamide **dextrans** inhibit breast cell growth
AU Bagheri-Yarmand, R.; Bittoun, P.; Champion, J.; Letourneur, D.; **Jozefonvicz, J.**; Fermandjian, S.; Crepin, M.
CS Institut d'Oncologie Cellulaire et Moleculaire Humaine (IOCMH), Bobigny, 93000, Fr.
SO In Vitro Cellular & Developmental Biology: Animal (1994), 30A(12), 822-4
CODEN: IVCAED; ISSN: 1071-2690
DT Journal
LA English
AB Several **dextran** derivs. were investigated to study the influence of substituents on their growth-inhibitory effects with HBL100 and HH9 cell lines. The chem. derivatization involved statistical distribution of chem. groups linked to the 1-6 glucosyl units forming the macromol. chains. Results showed that carboxymethyl groups linked to glucosyl units and benzylamide groups are required to promote cell growth inhibition.

L11 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1993:400364 CAPLUS
DN 119:364
TI Inhibitory effect of substituted **dextrans** on MCF7 human breast

cancer cell growth in vitro
AU Morere, J. F.; Letourneur, D.; Planchon, P.; Avramoglou, T.; **Jozefonvicz, J.**; Israel, L.; Crepin, M.
CS Serv. Oncol. Med., Hop. Avicenne, Bobigny, 93000, Fr.
SO Anti-Cancer Drugs (1992), 3(6), 629-34
CODEN: ANTDEV; ISSN: 0959-4973
DT Journal
LA English
AB Substituted **dextrans** can reproduce some of the properties of heparin and can thus be used to alter cellular growth. We studied the effect of heparin (H108), **dextran** (D), **carboxymethylbenzylamide dextran** (CMDB) and **carboxymethylbenzylamide** sulfonate **dextran** (CMDBS) on the growth of human mammary cells of the MCF7 tumor line. The cells were cultured in min. Eagle's medium contg. 2% fetal calf serum without biopolymer, or with increasing concns. of H108, D, CMDB or CMDBS. Growth curves were accurately based on cell counting using a Coulter counter. Cell distribution in the various phases of the cycle was analyzed by flow cytometry. Dose-dependent growth inhibitory effects (400-4000 .mu.g/mL) were obsd. The effect on MCF7 tumor cells was most apparent with CMDBS. The percentage of cells in the S phase decreased with preferential blocking in the G0/G1 phase. Pre-clin. studies can be anticipated as there is an absence of in vivo toxicity.

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FILE 'CAPLUS' ENTERED AT 11:56:13 ON 24 JUL 2003
L1 0 S DAHRICORREIA L?/AU
L2 178 S JOZEFONVICZ J?/AU
L3 189 S JOZEFOWICZ M?/AU
L4 291 S CORREIA J?/AU
L5 9 S HUYNH R?/AU
L6 0 S L1 AND L2 AND L3 AND L4 AND L5 AND DEXTRAN
L7 0 S L1 AND L2 AND L3 AND L4 AND L5 AND (DEXTRAN OR CMDBS OR DMCBS
L8 2 S L2 AND L3 AND L4 AND L5 AND DEXTRAN
L9 2 S L3 AND L4 AND L5 AND DEXTRAN
L10 90 S L2 AND DEXTRAN
L11 4 S L10 AND CARBOXYMETHYLBENZYLAMIDE

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